

### **REMARKS**

Claims 38-39, 41-42, 47, 50-57, 131-133, and 139-151 are pending with this amendment. Support for the amendments to the claims is replete throughout the application as filed.

Example support for the amendments to claim 38 are found at paragraphs 36, 66, 124 and 190-191. Example support for the amendments to claim 39 are found in original claims 40, and 43-46, as well as at paragraphs 35, 48, 165, and 175. Example support for the amendment to claims 42 and 47 is found at paragraphs 35, 44, 175, and in original claim 47. Example support for the amendment to claim 131 is found in original claim 120 and in paragraphs 35, 44 and 175. Example support for new claims 139-145 is found at paragraph 36, 66, and 190-191. Example support for new claim 146 is found at paragraphs 20, 121, 124, 282, 290, and in the figures and Examples. Example support for new claim 147 is found at paragraphs 45, 86-88, 124, 201, 282, and in the figures and Examples. Example support for new claim 148 at paragraphs 48, 92, 93, 95, 311, 315 and 318. Example support for new claims 149-150 is found at paragraphs 37 and 188. Example support for new claim 151 is found at paragraph 38. Additional support for the amendments and new claims is found throughout the application as filed.

The claims were rejected and objected to in the Action of May 9, 2007. Applicants traverse all rejections to the extent that they are applied to the amended claims, for the reasons noted herein. For convenience of the Examiner, Applicants' response addresses each rejection in the order presented in the Action of May 9.

### **PRIORITY**

Applicants thank the Examiner for acknowledging the priority claim.

### **INFORMATION DISCLOSURE STATEMENT**

Applicants thank the Examiner for considering the information disclosure statement of November 4, 2004.

### **OATH**

Applicants thank the Examiner for indicating that the oath is in compliance with 37 C.F.R. § 1.56.

## OBJECTIONS TO THE SPECIFICATION

Paragraphs [0184] (paragraph [0172] from the originally-filed application) and [0294] (paragraph [0272] from the originally-filed application) were objected to for including hyperlinks. Applicants have deleted the non-essential hyperlink information, overcoming the objection.

Paragraphs [0177] (paragraph [0168] from the originally-filed application) and [0181] (paragraph [0170] from the originally-filed application) were objected to for use of attorney docket information. These paragraphs have been updated with serial number information, overcoming the objection.

The Examiner further comments that the specification contains some redundancy, suggesting that redundancy should be avoided to reduce examination burden. No particular objection appears to be intended, and Applicants thank the Examiner for his suggestion. Applicants note that sections in the “Summary” of an application are typically expanded in the Detailed Description, which always results in a degree of redundancy between these sections. Applicants also note that the paragraphs cited in the Action do not correspond to the application as filed; if a formal objection is intended, Applicants request clarification of which paragraphs are involved in the objection.

## CLAIM OBJECTIONS

The Action objected to claims 38-57 and 131-133 for alleged lack of clarity in not specifying which residues of the relevant proteins could comprise unnatural amino acids, inquiring whether all residues could be made unnatural while retaining functional attributes of the protein. Applicants have amended the claims in part to address this objection.

With respect to claim 38, the amendment clarifies that the relevant GAL4 protein be at least 60% identical to a GAL4 protein that comprises both the DNA binding domain of wild-type GAL4 and the activation domain (see also, paragraph 124 of the application for a description of the relevant art-recognized domains of GAL4). Support for this amendment may be found, among other places in the specification, in paragraph [0037] of the published application, which is also known as paragraph [0036] of the originally-filed application.

With respect to the other pending claims, Applicants respectfully submit that it is reasonably clear from the claims that any protein that has the relevant unnatural amino acids and post-translational modifications is intended to be encompassed by the claims.

Accordingly, Applicants respectfully submit that the objection should be withdrawn.

#### REJECTION OF CLAIMS 48-49 UNDER 35 USC § 112, SECOND PARAGRAPH

Claims 48-49 were rejected for alleged indefiniteness for alleged lack of clarity. In the interest of expediting prosecution, these claims have been cancelled without prejudice, rendering the rejection moot.

#### REJECTION OF CLAIMS 38-57, 131-133 UNDER 35 USC § 112, FIRST PARAGRAPH

Claims 38-57 and 131-133 were rejected for alleged lack of enablement. To expedite prosecution, Applicants have amended the claims to address the issues raised in the rejection.

With respect to claim 38, the rejection argued that it was unclear which amino acids and what percentage of the relevant GAL4 could be modified. The claims have been modified to expressly recite that the relevant GAL4 mutants are at least 60% identical to a wild-type GAL4 protein comprising a DNA binding domain and an activation domain. Further, Applicants point out that GAL4 is one of the most completely studied proteins in modern molecular biology—the precise crystal structure for the protein is known, the DNA binding and activation domains are well-characterized, and the protein is routinely used as a reporter gene, making it amenable to super-high throughput activity screening. Accordingly, it is reasonable for one of skill to routinely modify this protein using the orthogonal systems of the invention, particularly when high throughput systems for screening for GAL4 activity are in such wide-spread use.

With respect to the other rejected claims, the relevant limitations of the claims require only that unnatural amino acids be encoded at one or more sites. This could be accomplished even with a single selector codon, unnatural amino acid, OtRNA and ORS. Put another way, any codon can be replaced with a selector codon, which can

be recognized by an OtRNA that is charged by an ORS with the unnatural amino acid, resulting in incorporation of a given unnatural amino acid at a site corresponding to the selector codon. This is all the teaching that the claims actually require.

Moreover, Applicants have provided a teaching of many different selector codons, including “e.g., nonsense codons, such as, stop codons, e.g., amber, ochre, and opal codons; four or more base codons; rare codons; codons derived from natural or unnatural base pairs and/or the like.” Specification, paragraph 71. Ways of making OtRNAs that specifically recognize these codons are specifically and accurately taught. Generic, high-throughput and broadly applicable ways of making ORS that specifically charge the OtRNAs are also taught, including hundreds of specific examples of appropriate unnatural amino acids, along with dozens of specific OtRNAs, ORS, and the like. Applicants’ methods of incorporating unnatural amino acids into proteins are generic, and are entitled to be claimed as such.

Accordingly, Applicants respectfully request that the rejection be withdrawn.

#### REJECTIONS PURSUANT TO 35 USC 102(E)—7,129,333

Claims 39-42, 45-57 and 131-133 were rejected for alleged anticipation by 7,129,333 (Schultz et al.). Applicants have amended the claims to render this rejection moot.

Specifically, claim 39 requires that the relevant protein additionally “comprises an oligosaccharide covalently coupled to an asparagine, threonine or serine residue of the protein.” Claim 42 requires, e.g., “wherein the modification is selected from the group consisting of: phosphorylation, lipid-modification, palmitoylation, palmitate addition and a glycolipid-linkage modification,” with claim 131 requiring similar language.

Applicants believe that the relevant claims are now novel over the relevant priority documents of 7,129,333, overcoming the rejection for alleged anticipation under 35 USC § 102(e). Applicants note that the ’333 patent has a common owner with the subject case and that the inventors were under a common obligation of assignment; accordingly, a rejection for alleged obviousness using the ’333 patent cannot be made, pursuant to 35 USC 103(c)(1).

Accordingly, Applicants respectfully request that the rejection be withdrawn.

REJECTION PURSUANT TO 35 USC § 102(B) KIGA ET AL. AND SAKAMOTO ET AL

Claims 38 and 131 were rejected for alleged anticipation by Kiga et al. and separately by Sakamoto et al. Applicants have amended the claims to render the rejection moot.

The crux of the rejection with respect to claim 38 was an argument that Kiga et al. and Sakamoto et al., which allegedly relate to incorporation of 3-iodo-L-tyrosine into c-Ha-Ras could be read on claim 38 due to the original breadth of the claim. Claim 38 has been amended to more particularly recite the structure of the GAL4 proteins being claimed; clearly, the c-Ha-Ras protein of Kiga et al. and Sakamoto et al. is not related to GAL4, and is not relevant to the amended claim.

Claim 131 now specifies that the relevant protein include a post-translational modification comprising a lipid-modification, palmitoylation, palmitate addition or a glycolipid-linkage modification. This limitation, among others, is not found in Kiga et al. or Sakamoto et al.

Accordingly, Applicants respectfully request that the rejection be withdrawn.

REJECTION PURSUANT TO 35 USC § 102(B) WANG ET AL.

Claims 131 and 132 were rejected for alleged anticipation by Wang et al. Applicants have amended the claims, overcoming the rejection. Specifically, claim 131 now recites that the relevant protein is post-translationally modified by lipid-modification, palmitoylation, palmitate addition or a glycolipid-linkage modification. This limitation is not taught in Wang et al.

Accordingly, Applicants respectfully request that the rejection be withdrawn.


CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the claims are deemed not to be in condition for allowance after consideration of this Response, an interview with the Examiner is hereby requested. Please telephone the undersigned at (510) 337-7871 to schedule an interview.

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Respectfully submitted,

  
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Attachments:

- 1) A petition to extend the period of response for **3** months;
- 2) A transmittal sheet;
- 3) A fee transmittal sheet;
- 4) Information Disclosure Statement;
- 5) International Search Report;
- 6) 1 Reference and,
- 7) A receipt indication postcard.